

A Model of Child Morbidity, Mortality and Health Interventions

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Abstract

A macro model of morbidity and mortality in children under five years of age is presented. Monthly disease-specific incidence and case fatality rates form the basis of the model and the efficacy and coverage of disease-specific interventions alter these values. In addition, frailty is modeled via relative risks of mortality based on five groups, determined in the first month by the birthweight distribution and at later ages by the proportion of children surviving a given illness who become more frail and the proportion not ill and with adequate nutrition who become less frail. A validation of the model was carried out using data from the comparison and treatment areas of the Demographic Surveillance System in Matlab, Bangladesh. The model very closely predicts the observed mortality level. Scenarios for improvements in coverage of specific interventions in settings in South Asia, West Africa and Andean South America are modeled and their effects on mortality gauged. The model provides a useful tool for those wishing to know the mortality impact of specified mixes of interventions in a given setting. Limitations of the model are considered and possible extensions to address these are discussed.

Infant and child mortality in many developing nations are very high due to frequent infectious diseases such as pneumonia and diarrhea (UNICEF, 1992). These deaths can be averted by interventions to prevent or treat the disease. For example, breastfeeding and clean water can help prevent diarrhea, while oral rehydration therapy (ORT) can reduce deaths among those who have diarrhea. Preventive interventions are usually broad-based at the community level, since all children must be covered, while curative interventions are applied to children with specific diseases.

The impact of any intervention depends upon the disease (or diseases) affected, the frequency of the disease(s) in the population, and the efficacy and coverage of the intervention. Preventive measures may have a greater impact on mortality than curative measures if they prevent multiple diseases. An example is vitamin A supplementation, which has been shown to protect children against death from multiple infectious diseases (Sommer 1986, Beaton et al. 1992). With respect to curative interventions, although their clinical efficacy may be known, it is unclear how much they can reduce mortality in a given community setting for two reasons--competing causes of death and frailty. For example, antibiotics can prevent a pneumonia death, but a child saved from pneumonia may succumb to a later episode

of diarrhea. Additionally, the pneumonia episode may have brought about reduced food intake leading to a decreased nutritional status (increased frailty), which puts the child at greater risk of mortality from subsequent infectious diseases.

A morbidity-mortality model that incorporated incidence, case fatality, interventions (and their associated costs), disease combinations, and competing risks was proposed by Barnum et al. (1980). An intended use of the model was to aid policymakers in finding cost-effective interventions. However, the model had several limitations. It relied heavily on subjective evaluations of the impact of interventions since empirical estimates of these were limited at the time that the model was developed. Also, it did not incorporate frailty. Furthermore, the model was complex and the computer software not generally available or easy to use. Another model that included incidence, case fatality, frailty and competing risks, but not efficacy and coverage of interventions was presented by Mosley and Becker (1991). In addition, any attempt to determine mortality trends in the 1990's needs to consider the effect of AIDS. Thus, to reasonably predict the impact of various health intervention strategies on infant and child mortality in developing nations, it was necessary to develop a new model.

THE MODEL

A macro-model of child mortality was designed to incorporate the following elements: disease-specific incidence and case fatality, frailty of children affecting the level of case fatality, with the frailty distribution of children at birth defined by the birthweight distribution, and frailty at later ages affected by cumulative disease insults and by the presence or absence of adequate nutrition or nutritional interventions; and health interventions to lower incidence and/or case fatality of selected diseases, with parameters for both efficacy and coverage of the interventions. Table 1 gives details of the diseases in the model and the interventions. In neonates, the specific causes of death are: 1) tetanus, 2) sepsis and pneumonia, 3) birth trauma and asphyxia, 4) diarrhea, 5) AIDS, and 6) all other causes. In those above one month of age, the causes are: 1) diarrhea, 2) respiratory disease (largely pneumonia), 3) malaria, 4) measles, 5) AIDS, and 6) other. Case fatalities due to AIDS and "other causes" are unaffected by frailty.

TABLE 1 ABOUT HERE

Figure 1 gives the flow of the model. The birth cohort starts with a given birthweight distribution, which can be modified in the model by nutritional interventions among mothers. Five frailty groups are defined with different relative risks of death¹. Age-specific disease incidence and case fatality in the

population are then adjusted by the efficacy and level of coverage of the interventions. Children who become ill are then subjected to the case fatality rate multiplied by the relative risk of death according to their frailty group. Children who survive the illness become more frail with a certain probability which depends on the illness; otherwise they remain in the same frailty group. A proportion of all surviving children are then shifted to a less frail group according to the proportion of children receiving an adequate diet and coverage of vitamin A supplementation. Surviving children enter the next age group and the process is repeated. The age interval for the model is a single month so the process is repeated sixty times. The one month interval was chosen in part to minimize the problem of multiple concurrent diseases. The latter are ignored by the model because the number of possible combinations of illnesses and the coverage and efficacy of interventions for them is very large and unwieldy.

FIGURE 1 ABOUT HERE

The proportion of newborns infected with HIV is determined by multiplying the prevalence in pregnant women by the probability of transmission to the newborn. Children with HIV are treated separately; they have a certain risk of dying of AIDS and are exposed to the same incidence and case fatality of other diseases

as other children. All of the children with HIV infection are assumed to die by age five (i.e. case fatality = 1.0 by the last age group).

After preparation of a flow chart, a specialized computer program was written in the FORTRAN language to perform the calculations, which simply involve addition and multiplication of the numerical input parameters. Appendix 1 gives the key equations. To check the results, a second programmer independently wrote a program in the C language. Outputs were compared and several minor programming errors were found in each program and corrected.

The main outputs of the model are age-cause-specific probabilities of death (q_x). Though estimates for single months of age are available, for most purposes the following age groups are considered: neonates, post-neonates, 12-23 months, 24-35 months, 36-47 months, 48-59 months. For infants, traditional neonatal and post-neonatal death rates are calculated using births as the denominator. For other age groups, cause-specific probabilities of death are calculated using the initial population in the age group as the denominator. We use the term mortality to refer to these probabilities. Sexes are combined.

Developing Country Settings Examined

Models were constructed for three developing country settings utilizing the best available information for each setting. The three were: A West African setting with high mortality and a high prevalence of malaria infection; a South Asian setting with high mortality and low prevalence of malaria; and an Andean South American setting with a moderately high level of mortality and a low prevalence of malaria. These settings are intended to be national in scale, but do not represent specific countries. Nevertheless, the availability of useful information from some countries, e.g. The Gambia (Greenwood et al. 1987a, 1987b) and Nigeria (Federal Office of Statistics, 1992) in West Africa, Bangladesh (Fauveau, 1994) in South Asia, and Peru (INEI, 1992) and Bolivia (Sommerfelt et al. 1991) in South America, allowed the model to be based largely on recently collected information concerning incidence and case fatality rates and the coverage of health and nutritional interventions. On the other hand, the efficacy inputs for the various interventions were generally based on the best evidence from developing countries as a whole.

For most of the diseases considered, it is difficult to determine the natural incidence in the absence of interventions such as good water, sanitation, breastfeeding, or good delivery practices. Therefore, information on the current incidence of diseases such as diarrhea, pneumonia, neonatal tetanus, or birth trauma/asphyxia, was used, along with the current coverage and

efficacy of interventions, to extrapolate back to the "natural" incidence in the complete absence of interventions. This incidence was then utilized as a starting point in the model. (See Appendix 1.) For malaria, a similar approach was used. The model treats the inputs as incidence, although the results might better be interpreted as reflective of the prevalence of malaria infection. We return to this point in the discussion.

Disease and Intervention Inputs in the Model

The incidence and case fatality rates for neonatal causes of death in the three settings are given in Table 2 as are the coverage of relevant interventions. The efficacies of interventions, assumed constant for all age groups and all settings, are given in Table 3. Table 4 shows the initial frailty groups defined by the birthweight distributions in the three settings, and the associated relative risks of mortality. Table 5 gives the estimated percentage of all children becoming more frail with a given disease and the percentage becoming less frail with a given intervention.

TABLE 2, 3 and 4 ABOUT HERE

For neonatal tetanus, the case fatality rate was set at 85%. All survivors become more frail. The interventions against neonatal

tetanus examined were two doses of tetanus toxoid during pregnancy, considered to have an efficacy of 80%, and good delivery practices with an efficacy of 50% (Schofield 1986). Given the limited resources in most developing country settings, an intervention to reduce case fatality from neonatal tetanus was not considered.

Neonatal deaths from birth injury, asphyxia, and other potentially preventable birth-related causes were grouped together (Partinidhi et al 1986, Shah 1990). Children surviving these conditions in the first month of life were considered to have a probability of shifting to a more frail group of 0.8 (Table 5). The intervention to prevent deaths in this group was good delivery practices, considered to have an efficacy of 50%.

TABLE 5 ABOUT HERE

For neonatal respiratory disease, the case fatality rate was set between 13% and 30% depending on the setting, with the higher rate in South America. For children surviving these conditions, the probability of becoming more frail is 0.3. The intervention for these conditions is antibiotic therapy, with an efficacy of 50%.

After the first month of life, the incidence of pneumonia was

estimated for each month of age from the best available community-based studies (Selwyn, 1990; Oyejide and Osinusi, 1990; Stewart, de Francisco and Fauveau, 1993). The incidence is highest in the youngest children and falls progressively with age.

With regard to interventions, breastfeeding is considered to protect against pneumonia. The efficacy of this protection was estimated at 50% for children 0-5 months of age and 25% thereafter (Victora, personal communication). Case management of pneumonia with appropriate antibiotics is considered to reduce the case fatality rate by 50% (Sazawal and Black, 1992).

Diarrheal diseases were included from the neonatal period onward. The diarrheal incidence rates were determined from community-based studies in the three settings (Black et al. 1982, Black et al. 1989; Oyejide and Fagbami, 1988). The rates increase during the first twelve months of life to a peak level between 12 and 17 months of age of 0.35 to 0.40 episodes per month. The rates fall progressively thereafter to a low of 0.25 per month. The case fatality rate is highest for diarrheal episodes during the neonatal period and drops progressively during the first year of life.

Two preventive interventions for diarrhea and one therapeutic

intervention were considered. Clean water and good sanitation together are considered to result in a 25% reduction of diarrhea incidence (Esrey, Feachem and Hughes, 1985). Breastfeeding during the first six months of life was estimated to have a 60% efficacy for prevention of diarrhea and a 25% efficacy after six months (Feachem and Koblinsky, 1984). For all diarrheal diseases, ORT was considered to have an efficacy of 30% (Richards et al. 1993). This rather low efficacy for ORT is the result of two factors. First, ORT given in the home, rather than in health facilities, may not be done optimally. For example, if it is given late or consumed in inadequate volumes, it may not prevent or correct dehydration that could lead to death. Second, ORT is primarily of value for acute dehydrating diarrheas that are now estimated to cause only 35-50% of all diarrhea-associated deaths (International Study Group on Mortality Due to Diarrhea, 1993). The remaining deaths, associated with dysentery or persistent diarrhea, are not greatly benefitted by ORT (Chowdhury et al. 1991). On the other hand, more comprehensive diarrheal management, including antibiotics for dysentery and dietary management of persistent diarrhea along with correctly used ORT, would be substantially more efficacious for all diarrheas. The efficacy of such comprehensive diarrheal treatment was considered to be 80%.

Malaria was considered to affect children after the neonatal

period. While the model incorporates incidence, the data available are for prevalence of parasitemia by age and are better regarded as such. The case fatality rate (percentage of children with parasitemia dying each month) was considered to be 1% in the three settings. The case fatality rate was applied to each month of age that a malaria infection was present.

The malaria interventions are treatment and prophylaxis. The decrease in the case fatality rate after presumptive treatment with chloroquin was considered to be only 20%. The efficacy is low because much of the presumptive self-treatment of fever with chloroquin is of questionable appropriateness and because of drug resistance to chloroquin (Greenwood et al 1988, World Health Organization 1990). The use of prophylactic chloroquin in children is infrequent (Institute of Medicine, 1991). In the model the presumptive treatment of fever with chloroquin was also considered like prophylaxis to reduce the incidence of infection with an efficacy of 50%. Thus, presumptive treatment had an effect on both the case fatality rate and on incidence.

The expected incidence of measles in the absence of measles vaccination was estimated from community-based studies (Dave 1983, McLean and Anderson 1988) and was assumed the same in all three settings. The incidence increases gradually from three to twelve months of age, reaching 3% per month, and then declines

after 23 months of age. These incidence values would result in 85% of children having measles before their fifth birthday. The case fatality rate was fixed at 2% in South Asia and South America and 4% in West Africa (Grabowsky et al. undated). Survivors from measles were also considered to have possible complications; the rate of diarrheal complications was estimated to be 30% and of pneumonia 10%. These complications had the same age-specific case fatality rates as for those diseases without measles.

The interventions for measles include both measles vaccine to reduce the incidence and therapy that could reduce the case fatality rate. With regard to the complications, the efficacy and coverage of ORT (or comprehensive diarrhea management) were assumed for treatment of the diarrhea associated with measles, and antibiotic efficacy and coverage were used for treatment of the pneumonia. In addition, vitamin A was considered to have an overall effect on measles case fatality with a 30% efficacy. (Hussey and Klein, 1990).

Other causes of death, including injuries, were considered as a group and were treated differently for the newborn period and subsequent periods. During the neonatal period, since there is a substantial amount of mortality associated with congenital abnormalities and other non-preventable conditions, mortality due

to other causes was estimated at five per 1000 in all settings.

For AIDS mortality, the proportion of pregnant women infected with HIV around 1990 was used (Preble 1990, Anderson and May 1992, Quinn et al. 1992). This was estimated to be 0.001 for South Asia and South America and .02 for West Africa. To determine the proportion of newborns developing HIV infection, this figure was multiplied by 0.3 for the apparent rate of transmission during pregnancy, childbirth or breastfeeding (Preble 1990). No intervention was considered for AIDS and all births with HIV were assumed to die by age five years.

Frailty Distribution and Frailty Factors

The initial frailty groups (Table 4) were determined utilizing the distribution of birthweights in each setting (World Health Organization 1984). Subsequent frailty groups were derived from the contribution of infectious diseases to increasing frailty and the effect of adequate diet or vitamin A supplementation in reducing frailty. The relative risks of death associated with the five frailty groups are 0.5, 1.0, 3.0, 5.0 and 10.0 (Victoria et al. 1988; Ashworth and Feachem, 1985; Pelletier, Frongillo and Habicht, 1993). For each disease, the proportions of children getting more frail due to the disease (Table 5) were estimated from studies evaluating the effect of these infections on

nutritional status (Black, Brown and Becker, 1984; Becker, Black and Brown, 1991). In the model, a child could change only one frailty group up or down in a month. The sensitivity of the results to the values of these frailty parameters is examined further below.

The interventions that could move children to a less frail group were adequate nutrition and vitamin A supplementation. Adequate nutrition was considered to be a composite of optimal energy intake, protein source (animal), and micronutrient intake appropriate for each age group. Children receiving at least the FAO/WHO requirements for age were considered to have adequate nutrition (WHO, 1985). For children with adequate nutrition, we estimated that 10% would switch to a less frail group in each month in the absence of a serious infectious disease. For vitamin A, the receipt of routine supplementation was considered sufficient to result in 10% of children switching to a less frail group each month. Children already receiving adequate nutrition were considered to have adequate vitamin A intake. Therefore, vitamin A supplementation had an effect on frailty only in children not receiving adequate nutrition.

Validation of the model

One might well ask to what extent the model gives a good approximation to reality. The inputs for the model are numerous, some estimates are known with poor precision and values of other parameters are virtually unknown (e.g. frailty factors) so it is important to assess the validity of the model in some way.

The extensive data available from the Demographic Surveillance System (DSS) in Matlab, Bangladesh provide an excellent opportunity for such a validation. In the Matlab area a rural population of 200,000 has been included in a vital registration system for more than twenty years. In 1978 the registration area was divided for program purposes into "treatment" and "comparison" areas with specific maternal and child health interventions added in the former area (Bhatia, Mosley and Faruque, 1980). In addition to vital registration data on births and deaths, data have also been collected on use of specific health interventions (Fauveau, 1994).

The procedure for validating the model with these data was as follows: First, estimates of input values for incidence and case fatality due to specific causes were derived for the comparison area for the period 1987-1990. Data on age-specific levels of intervention coverage were also available for that period (Table 6). These were entered in the model and are described more fully

in Appendix 2. The resulting outputs of infant and under-five mortality and the distribution by cause of death were compared to the actual values of these from the vital registration reports (ICDDR,B 1992, 1993 and 1994) for those years ²; the incidence and case fatality inputs were then adjusted until the observed and model mortality levels were virtually identical. These were used to generate the South Asian model.

TABLE 6 ABOUT HERE

Next the coverage levels of interventions were estimated from data for the "treatment" (health service intervention) area in Matlab (Table 6). These were entered in the model and all other parameters were the same as in the comparison area. The resulting mortality and cause of death distributions were compared with the observed values of these from the DSS data. Large differences between the predicted mortality and observed levels in the treatment area would show that the model was not valid; small differences would indicate that the model can produce valid results, at least for this setting.

Values of efficacies of interventions are those derived in the previous section and were identical in the two areas. Table 6 gives the age-averaged coverage of relevant interventions that varied between the two areas. For the comparison area the model

was calibrated to produce the observed levels of infant and under-five mortality of 92.5 and 135.5 deaths per 1000 respectively. The comparison of cause of death distributions is given in Table 7.

TABLE 7 ABOUT HERE

The changes in coverage of interventions to those of the treatment area produced output infant and under-five mortality levels of 78 and 106 per 1000 respectively. The actual values of these measures for the treatment area from published DSS reports were 77 and 103 per 1000 respectively. Thus, the model results were less than 3% different than the actual values. Note that the registered infant and under-five mortality levels were 16% and 22% lower in the treatment area than in the comparison area. We conclude that the present model can quite accurately reflect a real world situation.

Sensitivity Analyses

We did sensitivity analyses to determine to what extent the results are affected by the frailty parameters and changes in them. With the basic parameters in the South Asian model held fixed, we made the following changes in frailty: 1) Frailty was deleted from the model by setting all relative risks to 1.0; 2) The relative risks associated with the frailty groups were

altered to decrease the effect of frailty. Specifically, relative risks for the five groups were set at .75, 1.0, 2.0, 3.0 and 5.0 instead of .5, 1.0, 3.0, 5.0 and 10.0; 3) Relative to baseline levels, the proportions of children getting more frail with each disease were increased and decreased in separate runs by 25%; 4) The proportions of children getting less frail with adequate nutrition were increased and decreased in separate runs by 25%

With frailty eliminated, the model gives an estimate of under-five mortality that is 26% below the estimate with frailty included (Table 8). In the same vein, when the relative risks are brought closer to 1.0, mortality is also decreased.

When the proportions getting more frail due to diseases are changed by 25%, mortality changes by only 3%. On the other hand, when the proportions getting less frail due to adequate nutrition or vitamin A supplementation are changed by 25%, the results for mortality are 5% to 6% different from baseline levels. These larger changes in mortality compared to those when frailty parameters associated with disease were changed by the same percentage, occur because the nutritional effects apply to all children while the disease-specific frailty factors only apply to sick children. We conclude that frailty contributes significantly to mortality in the model but that the estimates

of mortality are relatively insensitive to errors in specification of the frailty parameters associated with diseases and nutrition.

TABLE 8 ABOUT HERE

MODELING SCENARIOS OF HEALTH INTERVENTIONS

Eleven intervention scenarios were evaluated for their effect on under-five mortality (${}_5q_0$); changes were made in the intervention efficacies and/or coverages fixing other parameters at their baseline levels for the three settings.

The World Summit for Children in 1990 established a list of goals for the year 2000 (UNICEF, 1991). These included reduction of overall under-five death rates by one third, reduction of diarrheal deaths by one half, and respiratory deaths by one third, elimination of neonatal tetanus, and reduction in measles deaths by 95%. The Summit also established targets for immunization coverage. WHO and UNICEF have established service delivery targets that they feel are achievable and should result in mortality reductions commensurate with the Summit goals. These service delivery targets were utilized in the model to estimate their effect on child mortality. To estimate the effect of an increasing prevalence of HIV in adult women by the Year

2000, the proportion of pregnant women infected was estimated at 0.01 for that year in South Asia and South America, up from the baseline level of 0.001. In West Africa the proportion was changed from .02 to .10. Table 9 lists the eleven scenarios that were studied with the model. Mortality by age and cause was estimated for each scenario and compared to the results of the model using the baseline parameters in the three settings.

TABLE 9 ABOUT HERE

The results of the various scenarios of health interventions are given in Table 10. In general because the levels of coverage of interventions are initially higher in South America, implementation of a given scenario has less absolute and relative impact on mortality there than in West Africa and South Asia.

In South Asia the greatest single impact on mortality occurs when measles immunization is increased to 90% (scenario 4). In South America and West Africa, by contrast, vitamin A supplementation is predicted to have the greatest impact in reducing mortality (scenario 6). South Asia had less effect from vitamin A supplementation since the current level of supplementary coverage was considered to be 50%, whereas in the other two regions it was zero. Increasing good birthing practices to 80% and increasing coverage of good sanitation have similar and small effects in

South America and West Africa but increasing good birth practices has a greater effect in South Asia (scenarios 9 and 10).

In all three settings increasing ORT coverage to 80% alters mortality levels only slightly (scenario 2). This is due to the assumed low efficacy of ORT against all diarrheas. In all three settings, having comprehensive diarrheal treatment reduces mortality much more than increasing ORT coverage alone.

Table 11 gives further detail; it shows the percentage declines in cause-specific mortality in South Asia under the same scenarios. The effect of increasing tetanus toxoid from 20% to 90% is a 65% reduction in tetanus mortality (from 5.7 to 2.0 per 1000. Increasing measles vaccine coverage has a substantial impact on deaths attributed to diarrhea as well as those attributed to measles but it only has a minor effect on pneumonia mortality.

With the inclusion of increased AIDS incidence, the declines in mortality are reversed in West Africa as ${}_5q_0$ rises from 162 to 183 per 1000. In South Asia and South America the inclusion of AIDS changes mortality only slightly.

TABLES 10 AND 11 ABOUT HERE

Non-additive effects of interventions

In the presence of competing risks of illness and death it is clear that a given intervention will have an equal or greater impact on mortality in the absence of other interventions, than when other interventions are present. To explore this quantitatively, we ran the South Asian model for the individual components of scenarios in Table 9 and compared the difference between the mortality level with only the given intervention and the baseline mortality, with the difference between mortality levels with the addition of each successive component as shown in Table 10.³ These estimates are compared in Figure 2. The sum of the separate intervention effects would imply an overall under-five mortality decline of 58 per 1000 (a 43% decline). This is contrasted with a decline of 50 per 1000 predicted by the model with all the interventions introduced simultaneously. From the figure we see that the interventions on case fatality have similar effects on mortality whether introduced singly or with other interventions. However, the interventions on disease incidence (e.g. measles vaccine) and frailty (e.g. vitamin A) show a much greater impact when introduced singly into a population. One difference is in the opposite direction--the effect of increasing the efficacy of ORT from 30% to 80% in the model with cumulative interventions is greater than when it is introduced singly. This is because greater ORT efficacy is a

more potent intervention in combination with an increase in coverage of ORT (from 57% to 80%).

FIGURE 2 ABOUT HERE

DISCUSSION

The quantitative effects of health interventions in reducing total childhood mortality in developing nations are difficult to estimate. Recent studies have shown that vitamin A supplementation can reduce mortality rates in children 6-59 months old by approximately 20% in settings with relatively high mortality and vitamin A deficiency (Sommer et al. 1986; Beaton et al., 1992). Measles vaccine has been shown to lead to a similar level of reduction (Aaby et al. 1984; Clemens et al. 1988; Koenig et al. 1991) and it has been argued that ORT reduced overall infant and child mortality by more than 30% in Egypt (El-Rafie et al. 1990). With multiple interventions and multiple causes of death, the picture becomes complex, i.e. these separate effects cannot be added.

International health agencies and policy makers must decide on the interventions to emphasize in a given setting. The World Bank has recently outlined global health challenges (World Bank, 1993). Before calculations of cost-effectiveness can be made for

this purpose, models combining epidemiological and demographic parameters must be constructed so the effects of various mixes and levels of interventions in a given setting can be predicted. We have presented one such model in this paper.

The results from the model for South Asia clearly show that fairly large increases in intervention coverage do not necessarily lead to large decreases in mortality. For example, increasing ORT coverage from 57% to 80% in South Asia only drops diarrheal mortality by 3 per 1000. On the other hand, including comprehensive diarrheal treatment drops the diarrheal specific mortality 10 per 1000 from its initial level. This is because ORT alone only has 30% efficacy against diarrheal death while comprehensive treatment has an 80% efficacy.

The child survival interventions have been selected for widespread implementation because they address important causes of child mortality and indeed ORT and immunization programs have reduced mortality levels. However, it must be kept in perspective that these least costly interventions have limitations. Also there may be problems reaching children who are at highest risk of mortality.

Furthermore, the reductions in mortality from a very restricted set of interventions will be at best moderate in most settings,

even if they are delivered optimally. This speaks for the need to implement a complementary set of preventive and therapeutic interventions addressing the common causes of mortality in children - diarrhea, measles, tetanus, malaria and pneumonia. Such a package of interventions implemented with potentially achievable coverage levels could reduce child mortality by up to 40%, consistent with the UNICEF Summit targets. Interventions that reduce frailty should have substantial effects on mortality from various causes (Pelletier, Frongillo and Habicht, 1993). For example, increasing vitamin A coverage in the model from 50% to 80% decreases under-five mortality from 105 to 101 per 1000 in South Asia and the effect is even more in other regions with widespread deficiency and without supplementation programs.

This macro-model is a useful tool to study the effects of various interventions on child mortality. Of course, as in any such exercise, the results are highly dependent on the inputs and assumptions of the model. The best available data were used as inputs. However, as noted above, some parameters are not directly observable in the population, in particular the proportion of children becoming more frail with a given disease or less frail with nutritional interventions. From the sensitivity analyses we have shown that a 25% error in these frailty parameters would yield no more than 6% error in mortality. This is relatively small compared to the overall

effect of incorporating frailty in the model (i.e. a 26% difference in estimated mortality between models with and without frailty).

Generally, the model is very flexible in structure, allowing: a) six disease groups; b) incidence, case fatality and coverage of interventions that can vary with each month of age; c) explicit frailty effects depending on each disease and d) the efficacy of interventions that affect incidence or case fatality of diseases, or frailty. This permits the examination of a wide range of interventions either singly or in combination, while accounting for competing risks and frailty.

However, in some ways the model is restrictive: a) Having five frailty groups is arbitrary (although the number could quite easily be changed) and frailty-specific relative risks of death are assumed to be equal for all infectious diseases; b) Risks associated with multiple concurrent illnesses are not included⁴; c) Malaria is incorporated via incidence and case fatality rather than prevalence; d) Disease rates for children with HIV infection are assumed to be the same as those in the general population; e) The model presently assumes homogeneity although populations are actually heterogeneous with respect to incidence and case fatality of diseases and coverage of interventions⁵ and f)

Variances of estimates are not available since it is a macrosimulation rather than a microsimulation model. In addition, cost-effectiveness cannot be examined directly since cost estimates of interventions were not incorporated. The model could be further extended to remove most of these restrictions. Nevertheless, the present model can be very useful for providing estimates of the mortality effect of various interventions in specific settings ⁶.

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NOTES

¹ The number of groups was arbitrarily chosen.

² The values from the reports were averaged.

³ Malaria intervention was excluded from this analysis because it had a trivial effect in South Asia and AIDS prevalence for the year 2000 was excluded as well because it operates to increase mortality.

⁴ Similarly, considering in a sequential manner the proportions getting more frail from a given disease and then the proportion getting less frail because of good nutrition, gives different results than if these are considered simultaneously with the joint probability of the four possible outcomes [i.e. 1) illness makes the child more frail and this is not compensated by good nutrition; 2) illness makes the child more frail and this is compensated by good nutrition so the child stays in the same frailty group; 3) illness does not make the child more frail and good nutrition puts him/her in a less frail group; 4) illness does not make the child more frail and the absence of good nutrition means that he/she stays in the same frailty group.] Treating illness and nutrition interventions sequentially allowed us to consider all children in a frailty group (whether ill or not) with respect to nutrition interventions since the proportions with good nutrition or Vitamin A supplementation were assumed to be the same for both groups.

⁵ Further work is being done at Johns Hopkins University to include heterogeneity of risks and coverage levels.

⁶ The FORTRAN program for the model with the South Asian input data is available from the first author.